REMARKS

Status of the Claims

Claims 1-21 are pending. Claims 1-5 and 21 are withdrawn from consideration as being directed to a non-elected invention. Claims 6-20 are rejected. Claims 7 and 15 are cancelled. Claims 6 and 14 are amended.

The 35 U.S.C. §112, first paragraph rejections

Claims 6-20 are rejected under 35 U.S.C. §112, first paragraph, because according to the Examiner the specification, while being enabling for a method of detecting a level of free leptin and a kit for an assay of a level of free leptin in a sample from a human and ovine comprising contacting a sample with a chicken leptin receptor domain, does not reasonably provide enablement for a method for detecting a level of free leptin and a kit for an assay of a level of free leptin in a sample from any individuals comprising an avian leptin receptor binding domain. Applicant respectfully traverses the rejection.

The Examiner states that the recitation of "avian leptin receptor binding domain" in claims 6 and 14 is broader than is supported by the specification, because other avian leptin receptor binding domains may have different binding requirements from the chicken leptin receptor binding domain. The Examiner further mentions that the art is unpredictable for binding characteristics of leptin receptor binding domains for avian species other than chicken, and that the Applicant has not provided any working examples of binding of free leptin to avian leptin receptor binding domains other than chicken.

Claims 6 and 14 are amended to recite "chicken leptin receptor binding domain", and so accordingly claims 6-20 are enabled by the specification as to the binding of free leptin to a chicken leptin receptor binding domain.

The Examiner further states that while the claims are enabled as to the binding of the chicken leptin receptor binding domain to leptin in human or sheep serum, the claims are not enabled by the specification as to the binding of leptin from any mammalian source. The Examiner mentions that the specification does not provide guidance or direction for the binding of the chicken leptin receptor binding domain to free leptin from rat, mouse, porcine, or bovine serum samples, and that no working examples are provided.

The Applicant respectfully traverses the Examiner's rejection. The specification demonstrates the binding of human and ovine free leptin to chicken leptin receptor binding domain. The specification states that leptin shows high interspecies conservation, with the human leptin sharing up to 84% and 87% homology with rat and mouse leptin, respectively (see the Description of the Related Art, first paragraph). There is therefore sufficient guidance in the specification and the relevant art to enable one skilled in the art to make and use the invention as claimed. Given the high degree of homology among mammalian leptins, and the examples of the binding of two mammalian free leptins in the specification, one skilled in the art would have a reasonable expectation of success to be able to bind a mammalian leptin to a chicken leptin receptor binding domain. Procedures to show the binding of peptides to receptors are also well known in the art, so that one skilled in the art would have a reasonable expectation of success in making and using the invention as claimed, without an undue degree of experimentation

as the Examiner suggests. Additionally, procedures for the measurement of analytes present in various sample types by immunoassay are well known in the art, so that one skilled in the art could reasonably expect to make and use the claimed invention for measurement of free leptin in various samples from individuals, including serum samples.

The Examiner further states that the claim recitations drawn to a condition or disorder related to a level of free leptin are not enabled, because Applicants have not linked free leptin levels with any disorders, nor provided any examples measuring abnormal free leptin levels in serum samples associated with a disorder or pathological condition related to leptin metabolism.

The Applicant respectfully traverses the Examiner's rejection. The specification describes the relevance of free leptin to conditions and diseases known in the art. Leptin has been found to exist mainly in the free form in obese individuals, but in the bound form in lean individuals (see the Description of the Related Art, third paragraph, and Janeckova, Physiol. Res. 50: 443 (2001), page 444, second column, second full paragraph). Persons with inactivating mutations of the leptin receptor are morbidly obese, remain prepubertal, and have hypogonadotrophic hypogonadism (see Mantzoros, Ann. Intern. Med. 130: 671 (1999), page 674, second column, first-third paragraphs). Accordingly, the determination of free leptin levels would be of significant value in diagnostic and therapeutic applications related to leptin physiology.

Further, compliance with 35 USC 112, first paragraph, does not turn on whether an example is disclosed; an example may be working or prophetic. A working example is not required for enablement if the invention is disclosed in such a manner that one skilled in the art may practice it without an undue amount of experimentation. The present

specification describes evidence present in the relevant art that indicates that free leptin has an important role in conditions and diseases related to leptin physiology. Therefore, one skilled in the art would have a reasonable expectation that free leptin levels would be linked to such conditions and diseases, and that free leptin levels in serum samples would be associated with a disorder or pathological condition related to leptin metabolism.

Accordingly, the Applicant respectfully requests that the rejection of claims 6-20 under 35 USC 112, first paragraph, be withdrawn.

The 35 USC §103 rejections

Claims 6-20 are rejected under 35 USC 103(a) as being unpatentable over Kratzch et al. (2002) in view of Horev et al. (2000).

Kratzsch et al. teach the detection of free leptin levels in human serum using the human soluble leptin receptor binding domain to capture the free leptin in a human serum sample. In Kratsch, human recombinant leptin receptor binding domains were attached to a microtiter plate, and human serum samples were measured for free leptin using an enzyme-linked antibody against human leptin. Horev et al. disclose the amino acid sequence of the chicken leptin receptor, the sequence similarities between the chicken and mammalian leptin receptors, and the conservation of a Trp-Ser-X-Trp-Ser motif involved in leptin binding between the mammalian and chicken leptin receptor genes. The Examiner states that it would have been prima facie obvious for one of ordinary skill in the art at the time of the invention to use the chicken leptin binding domain of the leptin receptor as taught by Horev et al. in a method and kit for measuring free leptin in a sample from an individual. According to the Examiner, one of skill in the art would be

motivated to combine the teachings of Horev and Kratzsch because it would reduce cost and increase efficiency for making a kit to assay free leptin in samples from numerous different species.

Applicant respectfully disagrees with the Examiner. For an invention to be obvious under 35 USC 103, there must be a motivation to combine the references in order to arrive at the claimed invention. There is no teaching or suggestion present in Kratzsch or Horev that would provide such a motivation for one skilled in the art to combine a chicken leptin receptor binding domain taught in Horev with the assay for human leptin taught in Kratzsch.

Kratzsch teaches only an assay for human leptin, using the human leptin receptor binding domain to bind to and capture human leptin in serum samples or standards. Kratzsch does not teach or suggest that a leptin receptor binding domain from a species other than human could be used to bind to human leptin, or to bind to leptin from any other species.

Horev teaches the cloning of the chicken leptin receptor gene, and compares similarities in nucleotide and amino acid sequences between the chicken receptor and the leptin receptor from human, cow, rat and mouse.

Horev reports a low amino acid sequence similarity between the chicken and mammalian leptin receptor gene products of 49-51% identical amino acids plus conservative substitutions. This report teaches away from the claimed invention, in that the low amino acid similiarity between the chicken and mammalian receptors suggests to one skilled in the art that the chicken receptor binding domain would not be likely to bind to mammalian leptins. Horev reports the conservation between the chicken and

mammalian receptors of the amino acid motif implicated in leptin binding; however, there is no teaching that conservation of this motif is solely determinative of the ability of the leptin to bind to the receptor. Horev otherwise provides no teaching or suggestion that the chicken leptin receptor binding domain could be used in an assay to measure leptin.

Taken together, Kratzsch and Horev provide no motivation for one skilled in the art to combine the chicken leptin receptor binding domain from Horev with the human leptin assay from Kratzsch to arrive at the claimed invention. In the absence of such a motivation, the choosing of elements from references to reconstruct the invention constitutes the use of hindsight that is impermissible in making a rejection under 35 USC 103.

The Applicant additionally points out that the claimed invention produces the unexpected result that human leptin binds more strongly to the chicken leptin receptor binding domain than chicken leptin itself. This result is shown in the specification in Table 2, showing the kinetic constants for complex formation of the chicken leptin binding domains with human or chicken leptin. In contrast, one skilled in the art would expect that chicken leptin would bind most strongly to the chicken receptor binding domain. It would therefore be unobvious to one skilled in the art to substitute a chicken leptin binding domain for a human leptin binding domain to arrive at the claimed invention.

Accordingly, considering that the references cited by the Examiner provide no motivation to combine their teachings to arrive at the claimed invention, and the

unexpected result produced by the claimed invention, the Applicant respectfully requests that the rejection of claims 6-20 under 35 USC 103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed October 17, 2006. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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Diagnostic Systems Laboratories, Inc.
445 Medical Center Boulevard
Webster, TX 77598
(281) 332-9678
hsoehnge@dslabs.com

Holly O. Soehnge, Ph.D., J.D.
Registration No. 54,786
Counsel for Applicant